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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/867,159	LORIA ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *64-83* is/are pending in the application.

4a) Of the above claim(s) *64-73* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *74-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 64-83 are pending.

2. Claims 64-73 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

3. The following new grounds of rejections are necessitated by the amendment filed 3/17/05.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 74-77 and 79-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No 5,256,680 (of record, Oct 1993; PTO 892) in view of US Pat No 6,455,686 (of record, Sept 2002, PTO 892), US Pat No 5,433,948 (of record, July 1995; PTO 892) and US Pat No 5,820,862 (of record, Oct 1998; PTO 892).

The '680 patent teaches an anti-allergic pharmaceutical composition comprising an inhibitor of histamine synthesis, which is also a histidine decarboxylase inhibitor, such as α-fluoromethyhistidine combined with one or more antihistamine compound such as H1 or H2 receptor antagonist such as cimetidine, ranitidine, terfenadine, famotidine (see col. 11, lines 33-45, in particular). The term comprising is open-ended. It expands the claimed composition to

include additional compound to include the reference composition. The reference composition inherently has the same anti-allergic response given the ingredients in the claimed composition has the same ingredient and is for treating allergic disease (see col. 3, line 46-47, in particular). The reference composition comprising the reference inhibitor of histamine synthesis or histidine decarboxylase inhibitor is present from 0.5 to 50 mg or 1 mg to 10 mg which is between claimed range of 1 and 2000 or between 5 and 200 mg (see col. 6, lines 23-35, in particular). The reference composition is releasable in the mucosal form such as buccal administration, nasal administration that is known to skilled in the art of pharmacy (see col. 6, line 59-67, in particular).

The claimed invention as recited in claim 74 differs from the teachings of the reference only in that the anti-allergic pharmaceutical composition comprising an acarid allergen comprising the allergen encoded by the polynucleotide of SEQ ID NO: 1 or the allergen as shown in SEQ ID NO: 2, antihistamine, inhibitor of histadine decarboxylase and a pharmaceutically acceptable carrier instead of just antihistamine inhibitor and inhibitor of histadine decarboxylase and a pharmaceutically acceptable carrier.

The claimed invention as recited in claim 75 differs from the teachings of the reference only in that the anti-allergic pharmaceutical composition comprising an acarid allergen comprising the allergen encoded by the polynucleotide of SEQ ID NO: 1 or the allergen as shown in SEQ ID NO: 2, antihistamine, inhibitor of histadine decarboxylase and a pharmaceutically acceptable carrier wherein the acarid allergen is *D. Pteronyssinus*.

The claimed invention as recited in claim 76 differs from the teachings of the reference only in that the anti-allergic pharmaceutical composition comprising an acarid allergen comprising the allergen encoded by the polynucleotide of SEQ ID NO: 1 or the allergen as shown in SEQ ID NO: 2, antihistamine, inhibitor of histadine decarboxylase and a pharmaceutically acceptable carrier wherein the acarid allergen is *D. Farinae*.

The claimed invention as recited in claim 77 differs from the teachings of the reference only in that the anti-allergic pharmaceutical composition comprising an acarid allergen comprising the allergen encoded by the polynucleotide of SEQ ID NO: 1 or the allergen as shown in SEQ ID NO: 2, antihistamine, inhibitor of histadine decarboxylase and a pharmaceutically acceptable carrier wherein the acarid allergen is a cysteine protease.

The '686 patent teaches an anti-allergic pharmaceutical composition comprising an allergen such as high molecular weight *Dermatophagoides farinae* proteins from mite in

conjunction with other compound such as anti-histamines (column 42, lines 40-59, in particular) associated with a pharmaceutical acceptable vehicle such as phosphate buffered saline (PBS, see column 44, line 63 bridging column 45, line 1, in particular) in a controlled released formulation such as liposome, transdermal delivery systems, or osmotic pumps (See column 41, lines 20-33, in particular). The term "comprising" is open-ended. It expands the claimed allergen of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4 and SEQ ID NO: 6 to include additional amino acids at either or both ends to include the reference allergen from *Dermatophagoides farinae*. The reference composition obviously is capable of reduce an immune reaction such as immediate hypersensitivity response (See column 51, Table 2, lines 13-15, in particular). The reference pharmaceutical composition contains from about 0.5 ng to about 1 g per kg body weight (See column 42, lines 26-28, in particular). The '686 patent further teaches a composition comprising anti-inflammatory agent or compound such as peptides from IgE or IgE specific Fc receptors or antibodies capable of binding to IgE and blocks IgE binding to Fc receptors that drive immunoglobulin heavy class switching from IgE to IgG which inherently switch from Th2 to Th1 that reduce IgE synthesis in the upstream phase while the reference anti-histamine inhibits the histamine release in the down stream phase (See column 42, lines 45-49, in particular). The reference pharmaceutical composition is administered in form of subcutaneous, intradermal, intravenous, nasal, oral, transdermal and intramuscular routes (See column 42, lines 35-39, in particular). The reference pharmaceutical composition is useful to treat allergic hypersensitivity reactions to dust mite such as allergic asthma, allergic rhinitis, atopic and allergic eczema or to desensitize humans who are allergic to dust mite (See column 36, lines 31-36, column 42, lines 60-63, in particular). The reference pharmaceutical composition contains a quantity of 1×10^{-8} microgram to about 100 μg or from about $1x\ 10^{-7}$ μg to about 10 μg (See column 27, lines 31-34, in particular). Claim 81 is included in this rejection because the claimed limitations of 1 to 1500 μg or from 10 to 150 μg include the reference quantity of allergy.

The '948 patent teaches an anti-allergic pharmaceutical composition comprising various allergens such as *D. farinae* allergen comprises the amino acid sequence of SEQ ID NO: 2 and encoded by the polynucleotide sequence comprises SEQ ID NO: 1. The reference polypeptide is 100% identical to the claimed SEQ ID NO: 2 wherein the reference allergen obvious has at least one epitope of a cystine protease (see summary of invention, col. 5, lines 35-53, col. 7, lines 25-37, in particular). The reference *D. farinae* allergen is a cystine protease (see col. 7, lines 25-37, in particular). The reference allergen is useful for as common immunotherapeutic peptides to be

administered in treating allergic reaction to the two or more mite species which share the same epitope (see col. 10, lines 26-35, in particular).

The '862 patent teaches an anti-allergic pharmaceutical composition comprising various allergens such as *D. Pteronyssinus* and *D. Farinae* or combination of peptides from *D. Pteronyssinus* and *D. Farinae* for treatment of allergy (see entire document, abstract, summary of invention, in particular). The '862 patent teaches various T cell epitopes (peptide) from *D. Pteronyssinus* and *D. Farinae* and mixture of peptides comprises SEQ ID NO: 10, 23 and 40. The reference peptides of SEQ ID NO: 10, 23 and 40 contain the claimed peptide of SEQ ID NO: 3, SEQ ID: 4 and SEQ ID NO: 5, respectively. The term "comprising" is open-ended. It expands the claimed allergen to include additional amino acids at either or both ends to include the reference allergen. The reference pharmaceutical composition is administered by subcutaneous injection, transdermal application, oral administration (mucosal), inhalation (nasal spray) (see col. 16, lines 42-55, in particular). The reference composition wherein the allergen is present in an amount of about 20-500 μg (see col. 16, lines 60-63, in particular) which is within the claimed amount of 1 to 1500 μg. The reference about 20 μg is within the claimed range of 10 to 150 μg. The '862 patent also teaches polynucleotide sequence such as SEQ ID NO: 1 that that encodes the reference allergen comprises SEQ ID NO: 2 (see reference SEQ ID NO: 1, in particular). The term "comprises" is open-ended. It expands the claimed peptide at either or both ends to include the reference peptide. The '862 patent further teaches isolated nucleic acid molecule encoding the reference allergen in various vector such as pMSG vector (see col. 8, lines 67, in particular) pTRC vector (see col. 9, lines 3-39, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the anti-allergic pharmaceutical composition comprising an inhibitor of histamine synthesis such as α-fluoromethyhistidine, with one or more antihistamine compound such as H1 or H2 receptor antagonist such as cimetidine, ranitidine, terfenadine, famotidine as taught by the '680 patent and the allergen *Dermatophagoides farinae* proteins from mite as taught by the '686 patent or the allergen from mite such as *D. farinae* allergen comprises the amino acid sequence of SEQ ID NO: 2 as taught by the '948 patent or the various allergens such as *D. Pteronyssinus* and *D. Farinae*, combination of peptides from *D. Pteronyssinus* and *D. Farinae* as taught by the '862 patent for a method of treating allergic reaction or allergic hypersensitivity to mites as taught by the '680 patent, the '686 patent, the '948 patent and the '862 patent. From the combined teachings of the references, it is apparent that one of ordinary

skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to combine because the '680 patent teaches the combination of inhibitor of histamine synthesis, which is also a histidine decarboxylase inhibitor such as α-fluoromethyhistidine and one or more antihistamine compound such as H1 or H2 receptor antagonist such as cimetidine, ranitidine, terfenadine, famotidine is useful for treating allergic diseases (see col. 3, line 46-47, in particular). The '686 patent teaches the combination of allergen from *Dermatophagoides farinae* and anti-histamines are useful for treating allergic hypersensitivity reactions to dust mite such as allergic asthma, allergic rhinitis, atopic and allergic eczema or to desensitize humans who are allergic to dust mite (See column 36, lines 31-36, column 42, lines 60-63, in particular). The '948 patent teaches allergen such as *D. farinae* allergen comprises the amino acid sequence of SEQ ID NO: 2 that encoded by the polynucleotide sequence comprises SEQ ID NO: 1 is useful for treating allergy to the two or more mite species which share the same epitope (see col. 10, lines 26-35, in particular). The '862 patent teaches allergens such as *D. Pteronyssinus* and *D. Farinae* or combination of peptides from *D. Pteronyssinus* and *D. Farinae* are useful for treating allergy (see entire document, abstract, summary of invention, in particular). In re Kerkhoven, 205USPQ 1069 (CCPA 1980), recognized that "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose ... [T]he idea of combining them flows logically from their having being individually taught in the prior art" (see MPEP 2144.06).

7. Claim 78 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No 5,256,680 (of record, Oct 1993; PTO 892) in view of US Pat No 6,455,686 (of record, Sept 2002, PTO 892), US Pat No 5,433,948 (of record, July 1995; PTO 892) and US Pat No 5,820,862 (of record, Oct 1998; PTO 892) as applied to claims 74-77 and 79-83 mentioned above and further in view of US Pat No 4,302,458 (of record, Nov 1981, PTO 892).

The combined teachings of '680, the '686, the '948, and '862 patents have been discussed supra.

The claimed invention as recited in claim 78 differs from the teachings of the reference only in that the anti-allergic pharmaceutical composition comprising an acarid allergen comprising the allergen encoded by the polynucleotide of SEQ ID NO: 1 or the allergen as shown

in SEQ ID NO: 2, antihistamine, inhibitor of histadine decarboxylase and a pharmaceutically acceptable carrier wherein the histadine decarboxylase is tritoqualine.

The '458 patent teaches a pharmaceutical composition comprising tritoqualine which has been known for its anti-allergy properties and its derivative such as 458 L (See column 1, lines 11-13, in particular). The reference tritoqualine and 458 L are histamine decarboxylase inhibitors (See column 5, lines 3-10, Table, in particular) and are useful in treatment of allergy conditions such as pollinoses, uriticaria, eczema (See column 5, lines 30-33, claims 7-9, in particular). The '458 patent further teaches that the reference pharmaceutical composition can be administered orally, rectally, in a daily dosage of 20 to 500 mg and in the forms of tablets, pills, or suppositories wherein the reference dosage is within the claimed dosage of between 1 and 2000mg, or within the claimed dosage of from 5 to 200 mg (See column 5, lines 34-37, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the histidine decarboxylase inhibitor such as α-fluoromethyhistidine as taught by the '680 patent for the tritoqualine, which is also a histidine decarboxylase inhibitor as taught by the '458 patent for an anti-allergic pharmaceutical composition comprising an acarid allergen as taught by the '686, the '948, and '862 patents and antihistamine, inhibitor of histadine decarboxylase such as tritoqualine and a pharmaceutically acceptable carrier as taught by the '680 patent and the '458 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '458 patent teaches tritoqualine and 458 L are histamine decarboxylase inhibitor (See column 5, lines 3-10, Table, in particular) and they are useful in treatment of allergy conditions such as pollinoses, uriticaria, eczema (See column 5, lines 30-33, claims 7-9, in particular). In re Kerkhoven, 205USPQ 1069 (CCPA 1980), recognized that "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose ... [T]he idea of combining them flows logically from their having being individually taught in the prior art" (see MPEP 2144.06). In re Aller, 220 F2d 454,456,105 USPQ233; 235 (CCPA 1955). See MPEP § 2144.05 part IIA. Therefore, the claimed invention is an obvious variation of the reference teachings, absent a showing of unobvious differences.

8. Claim 74 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No 5,256,680 (of record, Oct 1993; PTO 892) in view of US Pat No 6,258,816 (of record, July 2001, PTO 892) or US Pat No. 5,827,852 (of record, Oct 1998, PTO 892) or US Pat No 6,319,513 (of record, Nov 2001, PTO 892) and US Pat No 5,433,948 (of record, July 1995; PTO 892) or US Pat No 5,820,862 (of record, Oct 1998; PTO 892).

The '680 patent teaches an anti-allergic pharmaceutical composition comprising an inhibitor of histamine synthesis, which is also a histidine decarboxylase inhibitor such as α-fluoromethyhistidine combined with one or more antihistamine compound such as H1 or H2 receptor antagonist such as cimetidine, ranitidine, terfenadine, famotidine (see col. 11, lines 33-45, in particular). The term comprising is open-ended. It expands the claimed composition to include additional compound to include the reference composition. The reference composition inherently has the same anti-allergic response given the ingredients in the claimed composition has the same ingredient and is for treating allergic disease (see col. 3, line 46-47, in particular). The reference composition comprising the reference inhibitor of histamine synthesis or histidine decarboxylase inhibitor is present from 0.5 to 50 mg or 1 mg to 10 mg which is between claimed range of 1 and 2000 or between 5 and 200 mg (see col. 6, lines 23-35, in particular). The reference composition is releasable in the mucosal form such as buccal administration, nasal administration that is known to skilled in the art of pharmacy (see col. 6, line 59-67, in particular).

The claimed invention as recited in claim 74 differs from the teachings of the reference only in that the anti-allergic pharmaceutical composition comprising an acarid allergen comprising the allergen encoded by the polynucleotide of SEQ ID NO: 1 or the allergen as shown in SEQ ID NO: 2, antihistamine is brompheniramine, cetirizine, fexofenadine, cyproheptadine, dexchlorpheniramine, hydroxyzine, ketotifen, loratidine, mequitazine, oxotomide, mizolastine, ebastine, astemizole, carbinoxamide, alimemazine, buclizine, cyclizine, hydrochlorate or doxylamine, an inhibitor of histadine decarboxylase and a pharmaceutically acceptable carrier instead of just antihistamine inhibitor and inhibitor of antihistamine, inhibitor of histadine decarboxylase and a pharmaceutically acceptable carrier.

The '816 patent teaches anti-allergy anti-inflammatory composition comprising an antihistamine such as cetrizine at a dose of 1.16mg/kg and an anti-leukotriene such as Nimesulide for asthma (See claims 1-6 of '816 patent, in particular). The '816 patent teaches various Histamine receptor antagonist such as cetirizine, fexofenadine, acrivastine, asthmizole, and

loratidine for treatment of allergic rhinitis as they are long acting and are free from sedative and anticholinergic effects (See column 4, lines 43-47, in particular). The '816 patent further teaches that cetirizine is very effective in inhibiting the cutaneous early and late phase response by inhibiting PAF and eosinophil recruitment in skin (See column 5, line 3-5, in particular).

The '852 patent teaches various pharmaceutical composition comprising various sedating antihistamine such as chlorpheniramine, brompheniramine dexchlorpheiramine, cyproheptadine, hydroxyzine, and various non-sedating antihistamine such as ketotifen, loratidine, oxatomide, astemizole, and ebastine for treating allergy (See summary of Invention, column 6, lines 5-20, claims 1, and 6-12 of '852 patent, in particular).

The '513 patent teaches various pharmaceutical composition comprising various sedating antihistamine and non-sedating antihistamines such as dexchlorpheniramine, cyproheptadine, fexofeadine, loratidine, ebastine, astemizole, hydrozyzine (See column 10, lines 55 bridging column 11, lines 1-2, in particular). The '513 patent teaches that the reference composition is administered usually from 0.5 mg/kg to about 500 mg/kg per day, which is equivalent to 25 mg to 50 mg for an average person of 50 kg. The '513 patent teaches that the reference composition is administered from about 1 mg/kg to about 300 mg/kg per day, which is equivalent to 50 mg to 15000 mg or preferably from about 5 mg/kg per day to about 200 mg/kg per day, which is equivalent to 250 to 10,000 mg per day (See column 16, lines 23-31, in particular).

The '948 patent teaches an anti-allergic pharmaceutical composition comprising various allergens such as *D. farinae* allergen comprises the amino acid sequence of SEQ ID NO: 2 and encoded by the polynucleotide sequence comprises SEQ ID NO: 1. The reference polypeptide is 100% identical to the claimed SEQ ID NO: 2 wherein the reference allergen obvious has at least one epitope of a cystine protease (see summary of invention, col. 5, lines 35-53, col. 7, lines 25-37, in particular). The reference *D. farinae* allergen is a cystine protease (see col. 7, lines 25-37, in particular). The reference allergen is useful for as common immunotherapeutic peptides to be administered in treating allergic reaction to the two or more mite species which share the epitope (see col. 10, lines 26-35, in particular).

The '862 patent teaches an anti-allergic pharmaceutical composition comprising various allergens such as *D. Pteronyssinus* and *D. Farinae* or combination of peptides from *D. Pteronyssinus* and *D. Farinae* for treatment of allergy (see entire document, abstract, summary of invention, in particular). The '862 patent teaches various T cell epitopes (peptide) from *D. Pteronyssinus* and *D. Farinae* and mixture of peptides comprises SEQ ID NO: 10, 23 and 40.

The reference peptides of SEQ ID NO: 10, 23 and 40 contain the claimed peptide of SEQ ID NO: 3, SEQ ID: 4 and SEQ ID NO: 5, respectively. The reference pharmaceutical composition is administered by subcutaneous injection, transdermal application, oral administration (mucosal), inhalation (nasal spray) (see col. 16, lines 42-55, in particular). The reference composition wherein the allergen is present in an amount of about 20-500 μg (see col. 16, lines 60-63, in particular) which is within the claimed amount of 1 to 1500 μg. The reference about 20 μg is within the claimed range of 10 to 150 μg. The '862 patent also teaches polynucleotide sequence such as SEQ ID NO: 1 that that encodes the reference allergen comprises SEQ ID NO: 2 (see reference SEQ ID NO: 1, in particular). The term "comprises" is open-ended. It expands the claimed peptide at either or both ends to include the reference peptide. The '862 patent further teaches isolated nucleic acid molecule encoding the reference allergen in various vector such as pMSG vector (see col. 8, lines 67, in particular) pTRC vector (see col. 9, lines 3-39, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the antihistamine compound such as H1 or H2 receptor antagonist such as cimetidine as taught by the '680 patent for the various antihistamine compound such as cetirizine, fexofenadine, acrivastine, asthmizole, or loratidine taught by the '816 patent, or the chlorpheniramine, brompheniramine dexchlorpheiramine, cyproheptadine, hydroxyzine, and various non-sedating antihistamine such as ketotifen, loratidine, oxatomide, astemizole, and ebastine taught by the '852 patent and '513 patent in combination with an acrid allergen as taught by the '948 patent and/or the '862 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '816 patent teaches that histamine receptor antagonist such as cetirizine, fexofenadine, acrivastine, asthmizole, and loratidine are useful for treatment of allergic rhinitis because they are long acting and are free from sedative and anticholinergic effects (See column 4, lines 43-47, in particular) and that cetirizine is very effective in inhibiting the cutaneous early and late phase response by inhibiting PAF and eosinophil recruitment in skin (See column 5, line 3-5, in particular). The '852 patent teaches that various sedating antihistamine such as chlorpheniramine, brompheniramine dexchlorpheiramine, cyproheptadine, hydroxyzine, and various non-sedating antihistamine such as ketotifen, loratidine, oxatomide, astemizole, and ebastine are useful for treating allergy (See summary of Invention, column 6, lines 5-20, claims 1,

and 6-12 of '852 patent, in particular). The '513 patent teaches dexchlorpheniramine, cyproheptadine, fexofeadine, loratidine, ebastine, astemizole, and hydrozyzines are nonsedating antihistamine \ (See column 10, lines 55 bridging column 11, lines 1-2, in particular). The '680 patent teaches an anti-allergic pharmaceutical composition comprising an inhibitor of histamine synthesis, which is also a histidine decarboxylase inhibitor such as α-fluoromethyhistidine combined with one or more antihistamine compound such as H1 or H2 receptor antagonist such as cimetidine, ranitidine, terfenadine, famotidine (see col. 11, lines 33-45, in particular) and are useful for treating allergic diseases (see col. 3, line 46-47, in particular). The '948 patent teaches allergen such as *D. farinae* allergen comprises the amino acid sequence of SEQ ID NO: 2 that encoded by the polynucleotide sequence comprises SEQ ID NO: 1 is useful for treating allergy to the two or more mite species which share the same epitope (see col. 10, lines 26-35, in particular). The '862 patent teaches allergens such as *D. Pteronyssinus* and *D. Farinae* or combination of peptides from *D. Pteronyssinus* and *D. Farinae* are useful for treating allergy or allergic reaction (see entire document, abstract, summary of invention, in particular). In re Kerkhoven, 205USPQ 1069 (CCPA 1980), recognized that "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose ... [T]he idea of combining them flows logically from their having being individually taught in the prior art" (see MPEP 2144.06). In re Aller, 220 F2d 454,456,105 USPQ233; 235 (CCPA 1955). See MPEP § 2144.05 part IIA. Therefore, the claimed invention is an obvious variation of the reference teachings, absent a showing of unobvious differences.

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

12. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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May 27, 2005

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